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09/744,658	05/30/2001	Barbara P. Wallner	10248/7014	3397

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 07/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,658	WALLNER, BARBARA P.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *2-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 7-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. Applicant's election of the method and composition using the -B(D_1)(D_2) compounds of claims 7 and 17 in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 2-6 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

> An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Applicant's claim for priority is objected to because it claims priority based upon PCT International application PCT/US99/18315 under both 35 U.S.C. 120 and 365(c). However, these sections of the statute are mutually exclusive, and the reference to 35 U.S.C. 120 should be deleted. Further, the claim for priority needs to be re-written as a single sentence.

Correction is required.

3. Claims 7, 8, 11, 17, 18, 20, and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. At claim 7, lines 10 and 14, and claim 8, line 6, where the claims recite "heteroatoms which can be N, S, or O", it is not clear if the heteroatoms are permitted to be other than N, S, or O. At claim 7 in the definition of the substituent J in the

phosphonate group formula, it appears redundant to state that J can be "O-alkyl, N-alkyl, or alkyl, each O-alkyl, N-alkyl, or alkyl containing 1-20 carbon atoms and, optionally, heteroatoms which can be N, S, or O" when J has already been defined as being "any number of C, H, O, S, or N atoms in any combination". At claim 7, page 25, line 3, the definition of R is unclear because of the confusing placement of the commas. It is unclear if "may be substituted or unsubstituted" modifies only the aryl group, the alkyl and the aryl group, or the following alphaketo ester, and it is unclear if the alphaketo ester is intended as a possible R substituent. Claim 8 is indefinite because it states that T can be a cyano group. However, claim 7, upon which claim 8 depends, does not permit T to be a cyano group. Claim 8's recitation that each R_1 and R_2 is H is redundant because this is already required by claim 7, upon which claim 8 depends. At claim 8, line 3, "the R group of" should be changed to "the group consisting of" so that standard Markush terminology is used. There is no antecedent basis in the claims for the phrase "the inhibitory compound" at claim 8, line 3. The independent claim uses the terminology "compound". Claim 8 indicates that D_1 and D_2 can independently be F or together can be a ring. However, claim 7, upon which claim 8 depends, requires these variables to be hydroxyl groups or groups which are capable of being hydrolyzed to hydroxyl groups. Accordingly, the definitions of D_1 and D_2 in claims 7 and 8 are contradictory. At claim 8, line 5, the word "independently" is indefinite because the choice for D_1 and D_2 is dependent upon the other - either both together form the ring, or both are F. It is not possible for one of these substituents to be F and for the other to form a ring. Claims 17 and 18 contain the same indefinite language that claims 7 and 8 contain. At claims 11 and 21, "Xaa" should be changed to "X", consistent with the terminology used in claims 9 and 19 upon which they depend, and

because claims 11 and 21 do not define the variable "Xaa". Claims 20 and 21 refer to the "method of claim 19"; however, claim 19 is drawn to a pharmaceutical composition, not a method.

4. Claims 7-9 and 17-19 are objected to because of the following informalities: At claim 7, page 25, line 5, a semicolon should be inserted after the chemical formula. At claim 8, line 2, the comma after "H" should be changed to a semicolon. At claim 8, lines 4 and 5, "D1" and "D2" should be changed to "D_1" and "D_2", consistent with the terminology established in claim 7. Claims 17 and 18 contain the same informalities that claims 7 and 8 contain. At claim 9, line 3, and claim 19, line 6, "is" should be inserted after "X". Appropriate correction is required.

5. Claims 8 and 18 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 8 and 18 recite that T can be a cyano group and that D_1 and D_2 can independently be F or together can be a ring. However, these possibilities are not encompassed by claims 7 and 17 upon which claims 8 and 18 depend.

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-19 and 21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,355,614. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '614 patent, drawn to compositions comprising cyclic Xaa-boroPro compounds, anticipate the instant claims. This rejection assumes that claim 21 was intended to be a composition rather than a method claim (see the above rejection under 35 U.S.C. 112, second paragraph).

7. Instant claims 1, 9-12, 14-16, and 19-21 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/097,376 because the '376 application, under the test of 35 U.S.C. 112, first paragraph, discloses the instant claimed invention. Instant claims 7, 8, 13, 17, and 18 are not deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/097,376 because the '376 application, under the test of 35 U.S.C. 112, first paragraph, does not disclose the compounds of instant claims 7 and 17 which comprise an $[X]_m$ group or which do not comprise a C=O group attached to the ring, does not disclose the phosphonate groups of claims 7 and 17 in which J can be any number of C, H, O, S, or N atoms, and does not disclose treating neoplasms or cancer as is recited in instant claim 13.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1, 7-9, and 13-19 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 93/08259. The WO Patent Application '259 teaches treating diseases mediated by DP-IV by administering an inhibitor, such as Ala-boroPro, optionally in combination with a pharmaceutically acceptable carrier or diluent. Administration can be oral or parenteral, and dosages can be 1-500 mg/kg/day. Diseases to be treated include autoimmune diseases and HIV infection. Ala-boroPro has a K_i in the nanomolar range. See, e.g., page 15, lines 20-33; page 21, lines 4-30, and claim 5.

10. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 93/08259 as applied against claims 1, 7-9, and 13-19 above, and further in view of the Snow et al article (J. Am. Chem. Soc., Vol. 116, pages 10860-10869). The WO Patent Application '259 teaches administering Ala-boroPro, but does not teach administering this compound in cyclized form. The Snow et al article (see, e.g., the Abstract) teaches that boronic acid dipeptides, such as Ala-boroPro, in aqueous solution are in equilibrium with their cyclized form. Therefore, inherently at least some cyclized Ala-boroPro will be administered in the method of the WO Patent Application '259. This rejection could be overcome, e.g., by amending claim 11 to recite that the cyclic Xaa-boroPro is in the form of a substantially pure preparation.

11. Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 93/08259 as applied against claims 1, 7-9, and 13-19 above, and further in view of the Shioda et al article (PNAS, Vol. 95, pages 6331-63360). The WO Patent Application '259

does not disclose that it operates by inhibiting the action of DP-IV on SDF-1. The Shioda et al article teaches that SDF-1 interferes with cellular infection of HIV-1 by blocking the interaction of HIV-1 with CXCR-4, and therefore inherently the DP-IV inhibitor of the WO Patent Application '259 will alter the activity of SDF-1 in the subject to the same extent claimed by Applicant because the same DP-IV inhibitor is being administered to the same subject to treat the same disease. Patentability is not conferred merely by determining a more complete mechanism by which a prior art method proceeds.

12. Claims 1, 7-10, and 13-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Huber et al (U.S. Patent No. 6,100,234). Huber et al teach treating HIV-infected patients by administering DP-IV inhibitors, especially Val-boroPro, optionally in combination with a pharmaceutically acceptable carrier. Administration can be oral or parenteral, and dosages can be 0.01-10 mg/kg per day. See, e.g., column 10, line 15 - column 12, line 36, and claims 4 and 13.

13. Claim 11 is rejected under 35 U.S.C. 102(e) as being anticipated by Huber et al (U.S. Patent No. 6,100,234) as applied against claims 1, 7-10, and 13-20 above, and further in view of the Kelly et al article (J. Am. Chem. Soc., Vol. 115, pages 12637-12638) or the Snow et al article (J. Am. Chem. Soc., Vol. 116, pages 10860-10869). Huber et al teach administering Val-boroPro, but do not teach administering this compound in cyclized form. The Kelly et al article (see, e.g., equation 1) and the Snow et al article (see, e.g., the Abstract) teach that boronic acid dipeptides, such as Val-boroPro, in aqueous solution are in equilibrium with their cyclized form. Therefore, inherently at least some cyclized Val-boroPro will be administered in the method of

Huber et al. This rejection could be overcome, e.g., by amending claim 11 to recite that the cyclic Xaa-boroPro is in the form of a substantially pure preparation.

14. Claim 12 is rejected under 35 U.S.C. 102(e) as being anticipated by Huber et al (U.S. Patent No. 6,100,234) as applied against claims 1, 7-10, and 13-20 above, and further in view of the Shioda et al article (PNAS, Vol. 95, pages 6331-63360). Huber et al do not disclose that they operate by inhibiting the action of DP-IV on SDF-1. The Shioda et al article teaches that SDF-1 interferes with cellular infection of HIV-1 by blocking the interaction of HIV-1 with CXCR-4, and therefore inherently the DP-IV inhibitor of Huber et al will alter the activity of SDF-1 in the subject to the same extent claimed by Applicant because the same DP-IV inhibitor is being administered to the same subject to treat the same disease. Patentability is not conferred merely by determining a more complete mechanism by which a prior art method proceeds.

15. Claims 17-19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by the Kelly et al article (J. Am. Chem. Soc., Vol. 115, pages 12637-12638). The Kelly et al article teaches a compound of formula 7, which is a cyclic Xaa-boroPro, dissolved in an aqueous buffer adjusted to pH=7.8. See, e.g., page 12637, column 2, last paragraph. The aqueous buffer of the Kelly et al article corresponds to Applicant's pharmaceutically acceptable carrier. With respect to Applicant's claim limitations "pharmaceutical" and "for treating a medical disorder in a subject mediated by chemokine inactivation", it should be noted that intended use limitations do not impart patentability to composition claims which are otherwise anticipated by the prior art.

16. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 99/28474. The WO Patent Application '474 teaches administering an inhibitor of dipeptidyl peptidase IV in order to inhibit chemokine processing, thereby accelerating

angiogenesis. A target of this process is heart tissue suffering from atherosclerotic disease. See, e.g., page 4, lines 20-25, and page 23, lines 15-22.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

July 30, 2003